



From the INTERNATIONAL SEARCHING AUTHORITY

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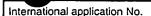
То:	
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ROBIC Attn. Orlhac, Thierry	INVITATION TO PAY ADDITIONAL FEES
55, rue St-Jacques Montréal, Québec H2Y 3X2 - 5 CANADA	(PCT Article 17(3)(a) and Rule 40.1)
- Ligen	
RAP 5 in	Date of mailing (day/month/year) 18/11/2003
Applicant's or agent's file reference	PAYMENT DUE
000711-0025	within 45 附近成为days from the above date of mailing
International application No.	International filing date
PCT/CA 03/00499	(day/month/year) 04/04/2003
Applicant	<u> </u>
UNIVERSITE DE MONTREAL	
This International Searching Authority (i) considers that there are	mber of) inventions claimed in the international application covered
and it considers that the international application does not (Rules 13.1, 13.2 and 13.3) for the reasons indicated the following the reasons indicated the r	t comply with the requirements of unity of invention W/on the extra sheet:
(ii) X has carried out a partial international search (see Annon those parts of the international application which related see annex (iii) will establish the international search report on the other particular particular search report on the other particular search report search report of the other search report search report search report search report search report s	to the invention first mentioned in claims Nos.:
to which, additional fees are paid	
2. The applicant is hereby invited, within the time limit indicated a	above, to pay the amount indicated below:
EUR 945.00 x3	= EUR 2.835,00
Fee per additional invention number of additional inv	ventions total amount of additional fees
Or,x	
The applicant is informed that, according to Rule 40.2(c), the pa i.e., a reasoned statement to the effect that the international app or that the amount of the required additional fee is excessive.	lyment of any additional fee may be made under protest, dication complies with the requirement of unity of invention
Claim(s) Nos. see annex Article 17(2)(b) because of defects under Article 17(2)(a) a	have been found to be unsearchable under under therefore have not been included with any invention.
lame and mailing address of the International Searching Authority	Authorized officer

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Jaap Hurenkamp





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This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-21; 37-40,41-44 partially

A stealthy polymeric biodegradable nanosphere comprising a polyester-polyethylene multiblock copolymer, use thereof for the preparation of a medicament, a method for delivering a pharmaceutical compound into a mammal by administration thereof, and method for preparation thereof.

2. Claims: 22-28

A polyester-polyethylene multiblock copolymer of formula (III): ABA-B'-(ABA-B')n-ABA (III), wherein A is a polyester, B is a polyethylene, B' is a dicarboxylic polyethylene and n>= 2. And a method for preparing the polyester-polyethylene multiblock copolymer of formula III.

3. Claims: 29-36

An improved method for preparing a PLA-PEG-PLA multiblock copolymer of formula (I): ABA-(c-ABA)n-c-ABA (I), wherein ABA is a PLA-PEG-PLA triblock, c is a carboxylic diacid, and n>=2.

4. Claims: 41-44 partially

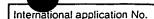
Method for preparing a stealthy polymeric biodegradable nanospheres from an emulsion, comprising the steps of (i) preparing an organic internal phase comprising a pharmaceutical compound and a blend of polymers and a polyester; (ii) preparing an aqueous external phase; (iii) injecting both phases into a homogenization chamber having an outlet; (iv) evaporating and/or extracting the phases of step (iii); collecting the stealthy polymeric nanospheres by centrifugation or dialysis.

The problem to be solved by the present application is a need for new stealthy polymeric biodegradable nanosphere compositions and polymers for synthesizing the same.

The solution proposed by the applicant is a stealthy biodegradable polyester-polyethylene multiblock copolymeric nanosphere.

A second solution proposed by the applicant is a polyester-polyethylene multiblock copolymer of formula (III): ABA-B'-(ABA-B')n-ABA (III).

A third solution proposed by the applicant is an improved method for preparing a polyester-polyethylene multiblock copolymer of formula (I):





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ABA-(c-ABA)n-c-ABA (I), wherein ABA is a PLA-PEG-PLA triblock.

A fourth solution proposed by the applicant is a method for preparing a stealthy polymeric biodegradable nanospheres comprising a blend of polymers and a polyester;

The idea to use polyester-polyethylene multiblock copolymeric nanospheres is already known from the following prior art documents:

D1: US6139870 (see whole document) discloses nanospheres comprising a PLA-PEG diblock copolymer and an anticancer agent.

D2: US5683723 (see whole document) discloses stealthy biodegradable nanospheres comprising a PLA-PEG diblock copolymer.

D3: W00112718 (see page 4, paragraph 4 - page 5, paragraph 1; page 5, last paragraph - page 6, paragraph 3; page 8, paragraph 2; page 10, paragraph 2, examples 10, and 11) discloses polymeric micelles of PEG-PLA-PEG or PEG-PLDO-PEG triblock copolymers and anticancer drugs.

D4: XP000783648 (see whole document) discloses nanospheres of PLA-POE-PLA triblock copolymer and progesterone.

D5: XP002257858 (see page 232, right-hand column, paragraph 3 - page 233, left-hand column, paragraph 2; page 235, left-hand column, last paragraph - right-hand column, paragraph 1) discloses nanospheres of polycaprolactone-PEG-polycaprolactone triblock copolymers and clonazepam.

D6: (see whole document) XP002257860 discloses nanospheres comprising PLA-PEG copolymer and an anticancer drug.

The idea to use polyester-polyethylene multiblock copolymeric nanospheres could no longer function as a special technical feature, and therefore as a single general inventive concept. In the present application, no further technical feature can be distinguished that can be regarded as a "special technical feature" involved in the technical relationship among the different inventions. Each of the invention listed above is a distinct invention, characterized by its own technical feature, defining the contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

The application relates to a plurality of inventions, or groups of inventions, in the sense of Rule 13.1 PCT. They have been divided as defined above. If the applicant pays additional fees for one (or more) not yet searched group(s) of invention(s), then the further search(es) may reveal further prior art that gives evidence of a further lack of unity 'a posteriori' within one (or more) of the not yet searched group(s). In such a case only the first invention in this (each of these) group(s) of inventions, which is considered to lack unity of invention, will be the subject of a search.

No further invitation to pay further additional fees will be issued. This is because Article 17(3)(a) PCT stipulates that the ISA shall establish the International Search Report on those parts of the international application which relate to the invention first mentioned in the claims



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('main invention') and for those parts which relate to inventions in respect of which the additional fees were paid. Neither the PCT nor the PCT guidelines provide a legal basis for further invitations to pay further additional search fees (W17/00, point 11 and W1/97, points 11-16).

International Application No. PCT&A 03 \(00499 \)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 206

Continuation of Box 3.

Although claims 21 and 37-40 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the composition.

COMMUNICATE RELATING TO THE RESULTS OF THE PARTINETERNATIONAL SEARCH



- 1.The present communication is an <u>Annex</u> to the invitation to pay additional fees (Form PCT/ISA/206). It shows the results of the international search established on the parts of the international application which relate to the invention first mentioned in claims Nos.:
- see 'Invitation to pay additional fees' 2. This communication is not the international search report which will be established according to Article 18 and Rule 43.
- 3.If the applicant does not pay any additional search fees, the information appearing in this communication will be considered as the result of the international search and will be included as such in the international search report.
- 4.If the applicant pays additional fees, the international search report will contain both the information appearing in this communication and the results of the international search on other parts of the international application for which such fees will have been paid.

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 139 870 A (VERRECCHIA THIERRY) 31 October 2000 (2000-10-31)	1-3, 13-17, 19-21, 37-39
	the whole document	
X	US 5 683 723 A (BAZILE DIDIER ET AL) 4 November 1997 (1997-11-04) the whole document	1-3, 13-21, 37-39,41
X	WO 01 12718 A (SEO MIN HYO; CHOI IN JA (KR); SAMYANG CORP (KR)) 22 February 2001 (2001-02-22) page 4, paragraph 4 -page 5, paragraph 1 page 5, last paragraph -page 6, paragraph 3 page 8, paragraph 2 page 10, paragraph 2; claims 1,3,6,19,12,15,16,18; examples 10,11	1-3, 13-17, 20,21, 37,39

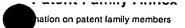
Further documents are listed in the continuation o	f box C.

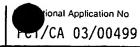
Patent family members are listed in annex.

- "A" document defining the general state of theart which is not considered to be of particular relevance
- "E" earlier document but published on or after theinternational filing date
- "L" document which may throw doubts on priority chirn(s) or which is cited to establish the publicationdate of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the internationalfiling date but later than the priority date claimed
- "T" later document published after theinternational filing date or priority date and not in conflict with theapplication but cited to understand the principle or theoryunderlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu ments, such combination being obvious to aperson skilled in the art.
- "&" document member of the same patent family

^{*} Special categories of cited documents :

Category °	NAKADA Y ET AL: "LONG-CIRCULATING NANOPARTICLES USING BIODEGRADABLE ABA TRIBLOCK COPOLYMERS CONTAINING POLY(L-LACTIC ACID) A-BLOCKS ATTACHED TO CENTRAL POLY(OXYETHYLENE) B-BLOCKS" PHARMACEUTICAL SCIENCES, LONDON, GB, vol. 3, no. 10, October 1997 (1997-10), pages 479-481, XP000783648 ISSN: 1356-6881 the whole document RYU JAE-GON ET AL: "Clonazepam release from core-shell type nanoparticles of poly(epsilon-caprolactone)/poly(ethylene	1-3, 13, 15, 17, 13, 15, 17, 18, 18, 18, 18, 18, 18, 18, 18, 18, 18
X	NAKADA Y ET AL: "LONG-CIRCULATING NANOPARTICLES USING BIODEGRADABLE ABA TRIBLOCK COPOLYMERS CONTAINING POLY(L-LACTIC ACID) A-BLOCKS ATTACHED TO CENTRAL POLY(OXYETHYLENE) B-BLOCKS" PHARMACEUTICAL SCIENCES, LONDON, GB, vol. 3, no. 10, October 1997 (1997-10), pages 479-481, XP000783648 ISSN: 1356-6881 the whole document RYU JAE-GON ET AL: "Clonazepam release from core-shell type nanoparticles of	1-3, 13-21, 37-39,41
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-	glycol)/poly(epsilon-caprola ctone) triblock copolymers" INTERNATIONAL JOURNAL OF PHARMACEUTICS (KIDLINGTON), vol. 200, no. 2, 10 May 2000 (2000-05-10), pages 231-242, XP002257858 ISSN: 0378-5173 page 232, right-hand column, paragraph 3 -page 233, left-hand column, paragraph 2 page 235, left-hand column, last paragraph -right-hand column, paragraph	15-17, 20,21, 37-39
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X	US 6 007 845 A (GREF RUXANDRA ET AL) 28 December 1999 (1999-12-28) column 3, line 66 -column 4, line 22 column 6, line 63 -column 7, line 11 column 9, line 19 - line 39 column 12, line 65 -column 13, line 4 claims 6,8,10,11,13,14,20,24,26,28,29; example 20	1,3, 13-15, 17-21, 37,39,40





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